CLAIMS

I claim:

1. A method comprising

providing a collection of mutant polypeptides wherein the amino acid sequence of each mutant polypeptide differs in at least one position from a polypeptide of interest, and

identifying those mutant polypeptides within the collection that (1) have an alteration in antibody reactivity compared to the polypeptide of interest, and (2) retain at least one desired characteristic,

wherein alteration in the antibody reactivity is determined by exposing the mutant polypeptides to individual antibodies or antibody fragments that are monospecific for the polypeptide of interest.

2. The method of claim 1 wherein the collection of mutant polypeptides is provided by

mutagenizing nucleic acid encoding a polypeptide of interest, and

expressing the mutagenized nucleic acid to produce the collection of mutant polypeptides.

3. The method of claim 2 wherein the nucleic acid encoding the polypeptide of interest is mutagenized such that a collection of randomly mutagenized nucleic acids is produced which encodes a collection of randomly mutant polypeptides.

4. The method of claim 1 wherein either or both the antibody reactivity and the alteration in the antibody reactivity are associated with an undesirable immune response.

5. The method of claim 2 wherein the antibody reactivity is the undesirable immune response, wherein the undesirable immune response is mediated by the antibody reactivity, wherein the antibody reactivity is involved in the undesirable immune response, wherein the antibody reactivity is associated with the undesirable immune response, or a combination of these.

6. The method of claim 1 wherein the antibodies or antibody fragments that are monospecific for the polypeptide are either monoclonal antibodies derived from mammals or antibodies or antibody fragments derived from a combinatorial library.

7. The method of claim 6 wherein the antibodies or antibody fragments are antibody fragments derived from a combinatorial library.

8. The method of claim 1 wherein the antibody reactivity is reactivity to IgA antibodies, reactivity to IgD antibodies, reactivity to IgE antibodies, reactivity to IgG antibodies, or reactivity to IgM antibodies.

9. The method of claim 8 wherein the antibody reactivity is reactivity to IgE antibodies that are reactive to the polypeptide of interest.

10. The method of claim 9 wherein the desired characteristic is T cell activation.

11. The method of claim 9 wherein the desired characteristic is an immune characteristic involved in desensitization.

12. The method of claim 1 wherein identification of mutant polypeptides that have an alteration in antibody reactivity is carried out prior to, simultaneous with, or following identification of mutant polypeptides that retain the desired characteristic.

13. The method of claim 1 wherein the desired characteristic is a bioactivity present in the polypeptide of interest.

14. The method of claim 13 wherein the bioactivity is selected from the group consisting of enzymatic activity, receptor binding, anticancer activity, immunosuppressive activity, immunostimulatory activity, immune characteristic, alteration of the function of immune system cells, antibiotic activity, antiviral activity, and trophic activity.

15. The method of claim 14 wherein the bioactivity is T cell activation or B cell activation.

16. The method of claim 14 wherein the bioactivity is an immune characteristic involved in desensitization.

17. The method of claim 14 wherein the bioactivity is an alteration of the function of immune system cells, wherein the cells are dendritic cells, macrophages, mast cells, basophils, or eosinophils.

18. The method of claim 13 wherein the polypeptide of interest is a viral protein and wherein the bioactivity is mediation of viral assembly and infectivity or cell-entry.

19. The method of claim 1 further comprising

identifying the mutations present in the identified mutant polypeptides, and

combining two or more of the identified mutations in a single mutant polypeptide.

20. The method of claim 1 further comprising expressing the polypeptide in a transgenic animal or plant.

21. The method of claim 20 wherein the polypeptide of interest naturally occurs in non-transgenic animals or plants of the same type as the transgenic animal or plant.

22. The method of claim 1 further comprising

administering one or more times to an individual one or more polypeptides each derived from at least one of the identified mutant polypeptides.

23. The method of claim 22 wherein each of the one or more polypeptides is one of the identified mutant polypeptides or a polypeptide combining mutations from two or more of the identified mutant polypeptides.

24. The method of claim 22 wherein the polypeptide is administered in combination with an immunomodulatory molecule.

25. The method of claim 24 wherein the polypeptide and immunomodulatory molecule are physically associated.

26. The method of claim 25 wherein the polypeptide and immunomodulatory molecule are co-encapsulated, covalently associated, or non-covalently associated.

27. The method of claim 26 wherein the polypeptide and immunomodulatory molecule are chemically coupled.

28. The method of claim 24 wherein the immunomodulatory molecule is a polypeptide fused to the polypeptide.

29. A polypeptide derived from at least one mutant polypeptide identified by the method of claim 1, wherein the polypeptide (1) has an alteration in antibody reactivity compared to the polypeptide of interest, and (2) retains the desired characteristic.

30. The polypeptide of claim 29 wherein the polypeptide is one of the identified mutant polypeptides or a polypeptide combining mutations from two or more of the identified mutant polypeptides.

31. The polypeptide of claim 29 wherein the mutant polypeptide has an alteration in at least one measurable immune characteristic associated with the undesirable immune response,

wherein the measurable immune characteristic is reactivity to IgE antibodies that are reactive to the polypeptide of interest.

32. The polypeptide of claim 29 wherein the polypeptide is produced in a transgenic plant or animal.

33. A fusion protein comprising the polypeptide of claim 29 and a polypeptide that has immunomodulatory activity.

34. A composition comprising the polypeptide of claim 29 and an immunomodulatory molecule.

35. The composition of claim 34 wherein the polypeptide and immunomodulatory molecule are physically associated.

36. The composition of claim 35 wherein the polypeptide and immunomodulatory molecule are co-encapsulated, covalently associated, or non-covalently associated.

37. The composition of claim 36 wherein the polypeptide and immunomodulatory molecule are chemically coupled.

38. The composition of claim 34 wherein the immunomodulatory molecule is a polypeptide fused to the polypeptide.

39. A nucleic acid encoding the polypeptide of claim 29.

40. The nucleic acid of claim 39 wherein the nucleic acid comprises a vector for expression of the polypeptide in a recombinant host.

41. The nucleic acid of claim 40 wherein the polypeptide is expressed in a transgenic plant or animal.

42. A transgenic plant expressing the polypeptide of claim 29.

43. The transgenic plant of claim 42 wherein the polypeptide of interest naturally occurs in non-transgenic plants of the same type as the transgenic plant.

44. A transgenic animal expressing the polypeptide of claim 29.

45. The transgenic animal of claim 44 wherein the polypeptide of interest naturally occurs in non-transgenic animals of the same type as the transgenic animal.

46. A method comprising

providing a collection of mutant polypeptides wherein the amino acid sequence of each mutant polypeptide differs in at least one position from a polypeptide of interest, wherein the polypeptide of interest is an allergen, and

identifying those mutant polypeptides within the collection that (1) exhibit less of, or have less potential to exhibit, an allergic response than the polypeptide of interest, and (2) retain at least one desired characteristic.

47. The method of claim 46 wherein the collection of mutant polypeptides is provided by

mutagenizing nucleic acid encoding a polypeptide of interest, and

expressing the mutagenized nucleic acid to produce the collection of mutant polypeptides.

48. The method of claim 46 wherein identification of mutant polypeptides that exhibit less of, or have less potential to exhibit, an allergic response is accomplished by exposing the mutant polypeptides to individual IgE antibodies or antibody fragments that are reactive to the polypeptide of interest.

49. The method of claim 48 wherein the IgE antibodies or antibody fragments that are reactive to the polypeptide of interest are either monoclonal IgE antibodies derived from mammals or IgE antibodies or antibody fragments derived from a combinatorial IgE library.

50. The method of claim 49 wherein the IgE antibodies or antibody fragments are IgE antibody fragments derived from a combinatorial IgE library.

51. ~~The method of claim 46 wherein the desired characteristic~~ is T cell activation.

52. The method of claim 46 wherein the desired characteristic is an immune characteristic involved in allergic desensitization.

53. The method of claim 46 wherein identification of mutant polypeptides that exhibit less of, or have less potential to exhibit, an allergic response is carried out prior to, simultaneous with, or following identification of mutant polypeptides ~~that retain the desired characteristic.~~

54. A method to treat an individual to reduce the allergic response to an allergen, the method comprising

administering one or more times to the individual one or more polypeptides each derived from at least one mutant polypeptide identified by the method of claim 46.

55. The method of claim 54 wherein each of the one or more polypeptides is one of the identified mutant polypeptides or a polypeptide combining mutations from two or more of the identified mutant polypeptides.

56. The method of claim 54 wherein the polypeptide is administered in combination with an immunomodulatory molecule.

57. The method of claim 56 wherein the polypeptide and immunomodulatory molecule are physically associated.

58. The method of claim 57 wherein the polypeptide and immunomodulatory molecule are co-encapsulated, covalently associated, or non-covalently associated.

59. The method of claim 58 wherein the polypeptide and immunomodulatory molecule are chemically coupled.

60. The method of claim 56 wherein the immunomodulatory molecule is a polypeptide fused to the polypeptide.

61. A method comprising

providing a collection of mutant polypeptides wherein the amino acid sequence of each mutant polypeptide differs in at least one position from a polypeptide of interest,

wherein each mutant polypeptide is part of a fusion polypeptide comprising the mutant polypeptide and a reporter protein, and

identifying those mutant polypeptides within the collection that (1) exhibit less of, or have less potential to exhibit, at least one undesirable immune response than the polypeptide of interest, and (2) retain at least one desired characteristic, and identifying fusion proteins with a functional reporter protein.

62. The method of claim 61 wherein the collection of mutant polypeptides is provided by

mutagenizing nucleic acid encoding a polypeptide of interest, and

expressing the mutagenized nucleic acid to produce the collection of mutant polypeptides,

wherein the mutagenized nucleic acid is operably linked to nucleic acid encoding the reporter protein such that the linked nucleic acids encode the fusion polypeptide comprising a mutant polypeptide and the reporter protein.

63. The method of claim 61 wherein identification of mutant polypeptides that exhibit less of, or have less potential to exhibit, the undesirable immune response is accomplished by identifying an alteration in at least one measurable immune characteristic associated with the undesirable immune response,

wherein either or both of the measurable immune characteristic and the alteration in the measurable immune characteristic are associated with the undesirable immune response.

64. The method of claim 63 wherein the measurable immune characteristic is antibody reactivity.

65. The method of claim 64 wherein the alteration in the measurable immune characteristic is a reduction in antibody reactivity.

66. The method of claim 64 wherein alteration in the measurable immune characteristic is determined by exposing the mutant polypeptides to individual antibodies or antibody fragments that are reactive to the polypeptide of interest,

wherein the antibodies or antibody fragments that are reactive to the polypeptide are either monoclonal antibodies derived from mammals or antibodies or antibody fragments derived from a combinatorial library.

67. The method of claim 66 wherein the antibodies or antibody fragments are antibody fragments derived from a combinatorial library.

68. The method of claim 64 wherein the measurable immune characteristic is reactivity to IgA antibodies, reactivity to IgD antibodies, reactivity to IgE antibodies, reactivity to IgG antibodies, or reactivity to IgM antibodies.

69. The method of claim 68 wherein the measurable immune characteristic is reactivity to IgE antibodies that are reactive to the polypeptide of interest.

70. The method of claim 69 wherein alteration in the measurable immune characteristic is determined by exposing the mutant polypeptides to individual IgE antibodies or antibody fragments that are reactive to the polypeptide of interest,

wherein the IgE antibodies or antibody fragments that are reactive to the polypeptide of interest are either monoclonal IgE antibodies derived from mammals or IgE antibodies or antibody fragments derived from a combinatorial IgE library.

71. The method of claim 70 wherein the IgE antibodies or antibody fragments are IgE antibody fragments derived from a combinatorial IgE library.

72. The method of claim 69 wherein the desired characteristic is T cell activation.

73. The method of claim 69 wherein the desired characteristic is an immune characteristic involved in desensitization.

74. The method of claim 63 wherein the measurable immune characteristic is T cell activation, B cell activation, NK cell activation, or alteration of the function of dendritic cells, macrophages, mast cells, basophils, or eosinophils.

75. The method of claim 63 wherein the measurable immune characteristic is the undesirable immune response, wherein the undesirable immune response is

mediated by the measurable immune characteristic, wherein the measurable immune characteristic is involved in the undesirable immune response, wherein the measurable immune characteristic is associated with the undesirable immune response, or a combination of these.

76. The method of claim 61 wherein identification of mutant polypeptides that exhibit less of, or have less potential to exhibit, the undesirable immune response is carried out prior to, simultaneous with, or following identification of mutant polypeptides that retain the desired characteristic.

77. The method of claim 61 wherein the undesirable immune response is reactivity to IgA antibodies, reactivity to IgD antibodies, reactivity to IgE antibodies, reactivity to IgG antibodies, reactivity to IgM antibodies, B cell activation, T cell activation, NK cell activation, or a combination.

78. The method of claim 61 wherein the undesirable immune response is humoral immune response, cellular immune response, or allergic response.

79. A method comprising

providing a collection of mutant polypeptides wherein the amino acid sequence of each mutant polypeptide differs in at least one position from a polypeptide of interest, and

identifying those mutant polypeptides within the collection that (1) exhibit less of, or have less potential to exhibit, at least one undesirable immune response than the polypeptide of interest, and (2) retain at least one desired characteristic, and identifying fusion proteins with a functional reporter protein,

wherein identification of mutant polypeptides that exhibit less of, or have less potential to exhibit, the undesirable immune response is accomplished by identifying an alteration in a measurable immune characteristic other than antibody reactivity that is associated with the undesirable immune response.

80. The method of claim 79 wherein the collection of mutant polypeptides is provided by

mutagenizing nucleic acid encoding a polypeptide of interest, and

expressing the mutagenized nucleic acid to produce the collection of mutant polypeptides.

81. The method of claim 80 wherein the nucleic acid encoding the polypeptide of interest is mutagenized such that a collection of randomly mutagenized nucleic acids is produced which encodes a collection of randomly mutant polypeptides.

82. The method of claim 79 wherein either or both of the measurable immune characteristic and the alteration in the measurable immune characteristic are associated with the undesirable immune response.

83. The method of claim 79 wherein the measurable immune characteristic is T cell activation, B cell activation, NK cell activation, or alteration of the function of dendritic cells, macrophages, mast cells, basophils, or eosinophils.

84. The method of claim 79 wherein the undesirable immune response is a humoral immune response, a cellular immune response, or an allergic response.

85. The method of claim 79 wherein identification of mutant polypeptides that exhibit less of, or have less potential to exhibit, the undesirable immune response is carried out prior to, simultaneous with, or following identification of mutant polypeptides that retain the desired characteristic.

86. The method of claim 79 wherein the desired characteristic is a bioactivity present in the polypeptide of interest.

87. The method of claim 86 wherein the bioactivity is selected from the group consisting of enzymatic activity, receptor binding, anticancer activity, immunosuppressive activity, immunostimulatory activity, immune characteristic, alteration of the function of immune system cells, antibiotic activity, antiviral activity, and trophic activity.

88. The method of claim 79 further comprising

identifying the mutations present in the identified mutant polypeptides, and

combining two or more of the identified mutations in a single mutant polypeptide.